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EXAMINER
NICHOLS, CHRISTOPHER J

ART UNIT	PAPER NUMBER
1647	16

DATE MAILED: 05/16/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/724,961	SCHENK, DALE B.	
	Examiner	Art Unit	
	Christopher Nichols, Ph.D.	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 February 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-12, 14-15,and 19-30* is/are pending in the application.

4a) Of the above claim(s) *24,25 and 27-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12,14,15,19-23 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6 11 15* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

1. Applicant's election of Group I (claims 1-23 and 26) in Paper No. 10 (12 September 2002) is acknowledged. Claims **24, 25**, and **27-30** are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim.

Status of Application, Amendments, and/or Claims

2. The Preliminary Amendment received 18 February 2003 (Paper No. 14) has been entered in full. Claims 13 and 16-18 have been cancelled. Claims 1-12, 14-15, 19-23, and 26 are under examination.

Sequence Requirements

3. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825 for the reason(s) set forth below. This application discloses an amino acid sequence on Figures 19 and 20 without the appropriate SEQ ID NO. Correction is required.

Drawings

4. The drawings are objected to because Figure 10 contains two panels which must be labeled "10A" and "10B" in both the drawings and the specification. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance.

5. The drawing of Figure 11 is objected to because the figure lacks an appropriate legend which indicates the peptide treatment groups as indicated and described in the figure and specification, see in particular pp. 62-63 and brief description of the drawings, p. 7. A proposed drawing correction or corrected drawings are required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. Applicants may alternatively choose to amend the brief description of the drawings so that it clearly reflects the groups represented in the Figure. Such amendment would be considered an appropriate correction so as to obviate abandonment of the application.

Information Disclosure Statement

6. The information disclosure statements filed 24 September 2001 (Paper No. 6), 12 September 2002 (Paper No. 11), and 18 February 2003 (Paper No. 15) contains particular references **(#144, #161, #174, #186, #220, #222, #223, #224, #304)** which fail to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because they lack a relevant public availability date. Those references have been placed in the application file, but the information referred to therein has not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement

or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

Double Patenting

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

A rejection based on double patenting of the "same invention" type finds its support in the language of 35 U.S.C. 101 which states that "whoever invents or discovers any new and useful process ... may obtain a patent therefor ..." (Emphasis added). Thus, the term "same invention," in this context, means an invention drawn to identical subject matter. See *Miller v. Eagle Mfg. Co.*, 151 U.S. 186 (1894); *In re Ockert*, 245 F.2d 467, 114 USPQ 330 (CCPA 1957); and *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970).

A statutory type (35 U.S.C. 101) double patenting rejection can be overcome by canceling or amending the conflicting claims so they are no longer coextensive in scope. The filing of a terminal disclaimer cannot overcome a double patenting rejection based upon 35 U.S.C. 101.

7. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims **1-2, 4-8,** and **10-24** of copending Application No. 09/322289. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

8. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims **1-23** and **26** of copending Application No.

09/580015. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

9. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under 35 U.S.C. 101 as claiming the same invention as that of claims **1-41** of copending Application No. 09/724273. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented.

Non-Statutory Double Patenting Rejection

> The non-statutory double patenting rejection, whether of the obviousness-type or non-obviousness-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and In re Goodman, 29 USPQ2d 2010 (Fed. Cir. 1993).
>
> A timely filed terminal disclaimer in compliance with 37 CFR 1.321(b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78(d).
>
> Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

10. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-46** of Application No. 09/497552. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are either anticipated by, or would have been obvious over the '552 claims. Both instant claims and the '532 claims are drawn to a

use of an anti-Aβ antibody as a medicament for Alzheimer's. Instant claims recite administration of antibodies comprising antibodies immunospecific for Aβ as does the '552. Thus, it would have been *prima facie* obvious to the skilled artisan that the claims in both instant and the '552 application would fully encompass treatment of Alzheimer's disease. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

11. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **42** and **43** of Application No. 09/497553. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are either anticipated by, or would have been obvious over the '553 claims. Both instant claims and the '533 claims are drawn to a use of an anti-Aβ antibody as a medicament for Alzheimer's. Instant claims recite administration of antibodies comprising antibodies immunospecific for Aβ as does the '553. Thus, it would have been *prima facie* obvious to the skilled artisan that the claims in both instant and the '553 application would fully encompass treatment of Alzheimer's disease. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

12. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-24, 28-32** and **36-37** of Application No. 09/724495. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are either anticipated by, or would have been obvious over the '495 claims. Both instant claims and the '495 claims are drawn to a use of an anti-Aβ antibody as a medicament for Alzheimer's disease including a step of immunizing the patient with an Aβ peptide and drawing the antibodies from said patient for *ex vivo* administration. Instant claims recite administration of antibodies comprising antibodies

immunospecific for an epitope within residues 1-5 of Aβ as does the '495. Thus, it would have been *prima facie* obvious to the skilled artisan that the claims in both instant and the '495 application would fully encompass treatment of Alzheimer's disease. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

13. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-47** of copending Application No. 09/979701. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are either anticipated by, or would have been obvious over the '701 claims. Both instant claims and the '495 claims are drawn to a use of an anti-Aβ antibody as a medicament for Alzheimer's disease including a step of immunizing the patient with an Aβ peptide and drawing the antibodies from said patient for *ex vivo* administration. Instant claims recite administration of antibodies comprising antibodies immunospecific for an epitope within residues 1-3, 1-4, 1-5, 1-6, 1-7, and 3-7 of Aβ as does the '701. Thus, it would have been prima facie obvious to the skilled artisan that the claims in both instant and the '701 application would fully encompass treatment of Alzheimer's disease. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

14. Claims **1-12, 14-15, 19-23,** and **26** are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims **1-41** and **44-47** of copending Application No. 09/580018. Although the conflicting claims are not identical, they are not patentably distinct from each other because instant claims are either anticipated by, or would have been obvious over the '018 claims. Both instant claims and the '018 claims are drawn to a use of an anti-Aβ antibody as a medicament for Alzheimer's disease. Instant claims recite administration of antibodies comprising anti-Aβ antibodies immunospecific for an epitope

within residues 1-12 of Aβ which is a genus for the species in the claims of '018 which are directed to an epitope within 1-3, 1-4, 1-5, 1-6, 1-7, and 3-7 of Aβ. Thus, it would have been prima facie obvious to the skilled artisan that the claims in both instant and the '018 application would fully encompass treatment of Alzheimer's disease. This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims **1-12, 14-15, 19-23,** and **26** are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for *treating Alzheimer's disease via administration of an anti-Aβ antibody that specifically binds to an epitope within residues 1-12 of Aβ,* does not reasonably provide enablement for *preventing or treating Down's syndrome, or preventing Alzheimer's disease or administration of an antibody that binds other components of an amyloid deposit.* The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to make and use the invention commensurate in scope with these claims.

16. The factors listed below have been considered in the analysis of enablement:

(A) The breadth of the claims;
(B) The nature of the invention;
(C) The state of the prior art;
(D) The level of one of ordinary skill;
(E) The level of predictability in the art;
(F) The amount of direction provided by the inventor;

(G) The existence of working examples; and
(H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

17. The instant invention is drawn to methods of treating amyloidogenic diseases comprising administration of an anti-Aβ antibody. The claims of the above invention are also drawn to methods of treating or preventing Down's syndrome or Alzhimer's Disease. Claims are presented which limited the antibody to those that bind an epitope within residues 1-12 of Aβ. The language of said claims encompasses both treatment and prevention.

18. The claims are drawn to a method for treatment and prevention of diseases associated with amyloid deposits of Aβ in the brain of a patient. The specification teaches that the administration of particular anti-Aβ antibodies is able to reduce β-amyloid levels within the brains of mice which are transgenic for PDAPP. These mice exhibit Alzheimer's type over production and build up of beta-amyloid within the brain. However, as recognized in the art, these mice do not exhibit Down's Syndrome or other amyloidogenic diseases, see in particular Schenk et al., Nature, 400:173-77, 1999 (**IDS**), Games et al. (9 February 1995) "Alzheimer-type neuropathology in transgenic mice overexpressing V717F β-amyloid precursor protein." Nature **373**(6514): 523-527 and Chen et al., Progress in Br. Res., 117:327-37, 1998 (**IDS**). Thus, the model system used is not recognized as providing for teachings that are predictive of the results which would be expected for the full scope of the claims. For example, the art recognizes that such *in vivo* models are not readily correlated to the human *in vivo* case. In particular, the art teaches a lack of correlation of beneficial effects shown in the mouse model system in humans; see in particular Münch & Robinson (July 2002) "Potential neurotoxic inflammatory responses

to Ab vaccination in humans." J. Neural Transmission 109(7-8): 1081-87. Thus, for the aforementioned reasons treatment of all amyloidogenic diseases or a treatment regiment that includes Down's syndrome and all other amyloidogenic diseases does not appear to be commensurate in scope with the claims (see Sipe (1992) "Amyloidosis" Annu. Rev. Biochem. **61**: 947-975).

19. Moreover, the model system does not fairly teach that the treatment is effective to prevent the onset of disease. Alternatively the teachings exhibit how one can reduce the pathogenic characteristics of Alzheimer-like pathology but fails to teach the prevention of plaque development in animals. As evidence, the Examiner notes that all PDAPP mice exhibited plaques regardless of treatment regime. Even the most effective treatments were only effective to reduce the plaque burden in animals, not prevent it.

20. While the use of anti-Aβ antibodies is feasible for treating Alzheimer's disease, as taught by Dodart et al. (March 2003) "Immunotherapy for Alzheimer's disease: will vaccination work?" TRENDS in Molecular Medicine **9**(3): 85-87 obstacles remain to successful practice of the instant invention (pp. 86-87). Furthermore Spooner *et al.* (13 December 2002) "The generation and characterization of potentially therapeutic Aβ antibodies in mice: differences according to strain and immunization protocol." Vaccine **21**(3-4): 290-297 teaches that the route of administration, the regiment of administration, and the genetic background of the mouse used affects the production of anti-Aβ antibodies in response to Aβ immunization (Table 1 and 2). It is also noted that although no deleterious effects were observed, this too could be dependent upon genetic factors of the animal receiving the immunization (pp. 296). Thus uncertainty is

found by use of Aβ as an immungen in regards to possible autoimmune reactions, general deleterious side effects, and variability in the production of anti-Aβ antibodies.

21. Finally the claims are drawn very broadly to methods of treating or preventing any condition or disease suspected of being associated with amyloid deposits. Since the specification fails to provide any guidance for the successful treatment or prevention of such a broad range of diseases, and since resolution of the various complications in regards to targeting a particular amyloid deposit in an organism is highly unpredictable, one of skill in the art would have been unable to practice the invention without engaging in undue trial and error experimentation. In order to practice the invention using the specification and the state of the prior art as outlined above, the quantity of experimentation required to practice the invention as claimed *in vivo* would require the *de novo* determination of formulations with acceptable toxicity and immunogenicity that are successfully delivered to target sites in appropriate cells and /or tissues. In the absence of any real guidance from the specification, the amount of experimentation would be undue, and one would have been unable to practice the invention over the scope claimed.

Claim Rejections - 35 USC § 102

22. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

23. Claims **1, 3, 6, 7, 8, 9, 10, 15,** and **19** are rejected under 35 U.S.C. 102(**b**) as being anticipated by Walker et al. (July 1994) "Labeling of Cerebral Amyloid In Vivo with a Monoclonal Antibody." Journal of Neuropathology and Experimental Neurology **53**(4): 377-383.

24. While not practicing the preamble of claim 1, Walker et al. are in fact practicing the relevant methods steps of administering an antibody that is immunospecific for Aβ with an epitope with residues 1-12 of said protein. The antibody used by Walker et al. is 10D5 whose epitope is defined as residues 3-6 of Aβ in the instant specification thus meeting the limitations of claims 1, 3, and 6 (Table 16). In addition, the instant specification discloses that 10D5 is an IgG1 monoclonal antibody and Walker et al. discloses that it is a whole antibody thus meeting the limitations of claims 1, 15, and 19 (Table 16; pp. 377 "Aβ Antibody and Nonimmune IgG). Further the monkeys used by Walker et al. are under 50 years of age and do not exhibit any signs of Alzheimer's disease thus meeting the limitations of claims 7, 8, and 10 (pp. 377 "Subjects"). While Walker et al. does not discloses any known risk factors, the monkeys are described as "aged nonhuman primates" of whom frequent develop Aβ deposits in their brains thus it could be construe that the monkeys do have an inherited risk factor for Alzheimer's disease, namely advanced age thus meeting the limitations of claims 9 and 10 (pp. 377).

25. In regards to the preamble's requirement of a therapeutic use, the specification discloses that 10D5 when administered to patients has a therapeutic effect of causing the phagocytosis of Aβ (Table 16; pp. 18-20, 93-99). It has been established by the courts that a product inherently possesses characteristics of that product (i.e. including the amino acid sequence of a protein). See, e.g., *Ex parte Gray*, 10 USPQ 2d; *In re Best*, 195 USPQ 430). In addition,

> "the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. Accordingly, since the

issue in the present appeal is whether the prior art factor is identified or patently indistinct from that of the material on appeal, appellants have the burden of showing that inherency is not involved". *Ex parte Gray*, 10 USPQ 2d 1922 (1989); *In re Best*, 195 USPQ 430 (CCPA 1976).

26. Moreover, when the product in a product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior art product was made by a different process. *In re Thorpe.*, 227 USPQ 964, 966 (Fed. Cir. 1985): *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983). Lastly it is noted that the courts have held that when the prior art product reasonable appears to be the same as that claimed, but differs by process in which it is produced, a rejection of this nature is eminently fair and the burden is upon the appellants to prove, by comparative evidence, a patentable difference (*In re Brown*, 173 USPQ 685).

Summary

27. Claims **1-12, 14-15, 19-23,** and **26** are rejected.

28. The following publications were found by the Examiner during the prior art search and are of note:

a. US 2002/0187157 A1 (12 December 2002) Jensen et al.

b. US 2002/0136718 A1 (26 September 2002) Raso

c. US 2002/0133001 A1 (19 September 2002) Gefter et al.

CONCLUSION

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Christopher James Nichols, Ph.D.** whose telephone number is 703-305-3955. The examiner can normally be reached on Monday through Friday, 8:00AM to 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Gary Kunz, Ph.D.** can be reached on 703-308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications. The fax phone numbers for the customer service center is 703-872-9305

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Elizabeth C. Kemmerer

CJN
May 8, 2003

ELIZABETH KEMMERER
PRIMARY EXAMINER